Dr. Ruth M. Lunn NIEHS P.O. Box 12233, MD K2–14 Research Triangle Park, NC 27709

Dear Dr. Lunn,

The Ajinomoto Company is one of the worlds leading manufacturers of aspartame. We take great pride in the quality and safety of the aspartame that we have manufactured since the early 1980s. We would like to take this opportunity to respond to the comment made about aspartame in the NTP "Draft Background Document for Formaldehyde".

The draft document asserts: "The artificial sweetener, aspartame consists of 10 percent methanol, which Humphries et al, (2008) reported can be converted to formaldehyde another derivatives. The authors also noted that research has shown that formaldehyde adducts accumulate in the tissues after aspartame ingestion".

The comment about aspartame as a source of formaldehyde adduct formation in body tissues is factually incorrect in the context of the existing literature on aspartame metabolism and current dietary exposure to the sweetener.

Aspartame is composed of the two amino acids, aspartic acid and phenylalanine plus a small amount of methanol and is completely hydrolyzed to the individual amino acids and a small amount of methanol in the lumen of the gastrointestinal tract. The 90th percentile of aspartame intake from all dietary sources is currently only 10mg kg day. (Magnuson et al., 2007). The amounts of the amino acids and methanol ingested from aspartame are insignificant when compared to other sources of those metabolites in the daily diet and are absorbed into general circulation, metabolized, utilized and excreted like any other dietary sources of those substances.

The methanol component of aspartame enters the portal circulation and is oxidized in the liver to formaldehyde via alcohol dehydrogenase. Human studies with aspartame have shown that no methanol accumulates in the blood. Furthermore, methanol is quickly metabolized to formaldehyde which has a half-life of only 1-2 minutes (MacMartin et al. 1979). No increase in formaldehyde has been detected in the blood after aspartame consumption (Tephly, 1999; Stegink et al. 1981, 1983).

Furthermore, formaldehyde enters the one-carbon pool of intermediary metabolism where it is metabolized to formate, an important substrate engaged in purine nucleotide synthesis. In fact it has been calculated over 50,000 mg of formaldehyde is produced and metabolized in adult human body daily and that human liver can metabolize 22mg of formaldehyde per minute (Magnuson et al. 2007).

Therefore, the lack of evidence of formaldehyde adducts formation from aspartame consumption clearly warrant removing the aspartame reference in the document. We thank you for considering our comments.

Sincerely,

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